REMARKS

Favorable reconsideration of the subject application, as amended above, is respectfully requested in view of the comments below.

Claims 54-106 are pending in the subject application. Claims 68, 86 and 96 are canceled herein. Claims 54, 65, 66, 67, 72, 85, and 95 have been amended to define the regulatory sequence as an enhancer sequence and/or to more particularly define the sequence as having been "obtained from" intron 3. These amendments are supported throughout the specification. Several of the claims have been amended to correct dependencies. A subset of the claims has been amended to change the language "adjacent to" to "operably linked" to more clearly define the location and functionality of the gene sequences. None of these amendments to the claims is substantive in nature and no new matter is added by these amendments.

The specification has been amended to add the sequence of the polynucleotide sequence incorporated by reference at page 5 of the specification (SEQ ID NO. 1). The addition of this sequence does not constitute new matter, since the sequence was originally incorporated by reference. The undersigned attorney avers that the material added in the sequence list is the same material incorporated by reference on page 5 of the specification, *i.e.*, Genebank accession number AF007544. SEQ ID NO. 1 was obtained by the undersigned attorney by printing out the sequence identified in the Genebank databank as AF007544. The specification has also been amended to provide a SEQ ID NO. for the sequence incorporated by reference on page 5. The specification complies with the requirements of an application containing a nucleotide and/or amino acid sequence 37 C.F.R. §§ 1.821 - 1.825.

Hereto is an attached Sequence Listing in paper and computer readable format. The paper copy and computer readable copy of the Sequence Listing are the same. The Sequence Listing does not include new matter.

It is brought to the Examiner's attention that the attorney docket number for the subject application has been changed. The new docket number is 64612-028.

I. Objections to the Specification and Claim 61

It is respectfully submitted that the addition of the sequence identifier, Seqence List, and amendment to claim 61 to correct dependencies renders the objections to the specification and claim 61 moot.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 54-59, 63-67, 72-78, 85, 90-95, and 100-106 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner states that the term "regulatory element" is broader than the written description.

It is respectfully submitted that the amendments to the claims render this ground of rejection moot.

III. Rejection of Claims Under 35 U.S.C. § 112, First Paragarph (Enablement)

Claims 85-106 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the enablement requirement. The Examiner states that the specification is enabling for *in vitro* embodiments of the claimed invention, but does not provide the person of skill in the art sufficient guidance to carry out the claimed invention commensurate in scope with the claims.

Applicants respectfully disagree with the Examiner's conclusion.

Claims 85-94 of the present application are directed to methods of obtaining expression of a coding sequence in a cell. These claims do not recite steps for treating disease, and indeed,

do not require that a therapeutic effect is obtained. All that is required is that the coding sequence is expressed in the cell, which has been sufficiently demonstrated in the specification, *i.e.*, Figures 5, 7, 9, 10 and 12, as well as Examples 4, 5, and 7-13. As can be seen from these examples and figures, gene expression using the claimed vector and enhancer element was demonstrated in a variety of cells.

Moreover, contrary to the Examiner's assertions, the specification discloses more than a single use for the claimed invention. The last paragraph on page four of the specification discloses that the regulatory regions of the invention "provide a target for the development of agents that may interfere with gene expression" in the target cells. This utility is accomplished by obtaining expression of the coding sequence in the cells into which it has been transfected. Thus, claims 85-94 are enabled by the specification.

Claims 95-106 are directed to methods of treating cancer. The specification provides several examples of the specificity of expression obtained with the claimed vectors and enhancer elements, and demonstrates that expression is obtained in a variety of cell types, including those cell types recited in claims 103-105, and at a variety of levels. Thus, the specification provides evidence of the functionality of the vector and enhancer elements for obtaining expression of a desired gene in cancer cells.

Further evidence of the ability of the claimed enhancer element to direct expression *in vivo* of a coding sequence to which it is operably linked is provided in the enclosed declaration of Peter Malloy, one of the co-inventors. The declaration describes experiments carried out in mice to test the efficacy of atadenovirus-delivered prostate-targeted gene-directed enzyme prodrug therapy in vivo. As set forth in the enclosed declaration, xenografts in nude mice were trasduced with the OadV63 virus vector encoding a purine nucleoside phosphorylae gene (PNP)

operably linked to the prostate-directed promoter and enhancer (PSMEPb). The results reported in the declaration demonstrate that the PNP gene was expressed in the xenografts and expression resulted in reduction of human prostate cancer xenografts mice in the mice. These results are direct evidence that the methods of claims 85-94, which require expression of a coding sequence operably linked to the enhancer sequencer are enabled. Furthermore, these results clearly demonstrate the efficacy of the methods of claims 95-106 for treating cancer *in vivo*.

The data shown in Figures 3A and 3B of the declaration demonstrate that intratumoral injection of the construct described above into xenografted nude mice results in expression the PNP gene and that such expression significantly reduces the rate of tumor growth of two distinct tumor types, *i.e.*, androgen-sensitive and androgen-refractory prostate cancer. As can be seen in Figures 4A and 4B, xenografted mice treated with the construct survived significantly longer than untreated mice.

The data present ed in the enclosed declaration demonstrate that the claimed construct is expressed *in vivo* and that such expression in tumor cells provides therapeutic effect. As such, the specification provides an enabling disclosure of claims 85-106.

Accordingly, the rejection of claims 85-106 under 35 U.S.C. § 112, first paragraph is respectfully traversed.

IV. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

It is respectfully submitted that the amendments to claims 54, 65, 72, 85 and 95 render the ground of rejection of these claims moot. It is further submitted that the amendments to claim 61 renders the ground of rejection of this claim moot. Similarly, the amendments to claims 65-66 render the ground of rejection of these claims moot.

In regards to the rejection of claims 62, 63, 69-71, 79, 80, 87-89, and 97-99, it is respectfully submitted that the definition of "high stringency conditions" provided at pages 8-9 of the specification is the standard definition, which is recognized by those of skill in the art. That the conditions vary according to the GC content of the sequence in question is known by those of skill in the art and is not "open to interpretation" as suggested by the Examiner. There is nothing vague or indefinite about the standard, art accepted definition of the hybridization conditions.

It is respectfully submitted that the ground of rejection of claims 62, 63, 69-71, 79, 80, 87-89, and 97-99 is respectfully traversed.

Accordingly, the rejection of claims 54, 61, 62, 63, 65, 72, 85, 95, 69-71, 79, 80, 87-89, and 97-99 is respectfully traversed.

It is respectfully submitted that the present application is in condition for allowance, an early notification thereof being earnestly solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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